

Nephroblastoma (Wilms' Tumor): Sex and Age Distribution and Correlation Rate with Ages, Sex, And Kidney Side in Sana'a City, Yemen

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Abstract

Wilms' tumor is a malignant tumor that contains metanephric blastema, stromal and epithelial derivatives. The characteristic is the presence of abortive tubules and glomeruli surrounded by the stroma of a spindle cell. The stroma may include striated muscle, cartilage, bone, adipose tissue, and fibrous tissue. The study aimed to describe the age, sex, and histology distribution of Wilms' tumor and its association with age groups, sex, and the side affected by the kidneys. A retrospective observational study was performed on renal masses patients who were consequently diagnosed selectively by histopathological study in the National Center for Public Health Laboratories (NCPHL) at the Department of Pathology, and the Department of Pathology in Al-Thorah university hospital, Sana'a, Yemen, over a period of 18 years from January 1, 2004, to December 31, 2021. Data were collected from hospital records. The study variables were lesions histological types, benign, malignancy, non-neoplastic lesions, sex, grades, and age. The whole data were analyzed by IBM SPSS Statistics 22. Ink. The outcomes for variables were given in the form of rates (%). Chi-Square was used for categorical variables that measured association among categorical variables. *P*-values less than 0.05 were considered significant. Wilms tumors count 47/282 (16.7%) of total diagnostic malignant tumors. The female cases were 29/47 (61.7%) more than male cases 18/47 (38.3%) with M: F ratio equal to 1.0: 1.6. The mean age of the Wilms' patients was 5.3 years with SD equal to 3.6 years and ages ranged from 9 months to 15 years. Most of the Wilms patients were in the age group 1-5 years 31/47 (66%) followed by 6-10 years (25.5%). Favorable histology (FVH) Wilms' tumors with better prognosis counting 42/47 (89.4%) while unfavorable histology (UFVH) with poor prognosis only counting 5/47 (10.6%). There was no significant association between Wilms' tumor and gender while there was a highly significant association of Wilms' tumor in the 1-5 years group (rate = 77.5%, OR=48.6, CI =19.8-119, *p* <0.001) and with 6-10 years group (rate= 80%, OR=26.6, CI=7.1 – 98.7, *p* <0.001). There was no significant association between Wilms' tumors with the kidney side in which roughly equal rates were present in both sides. Wilms' tumors in Yemeni children appear at an early age and peak in the first 5 years of life with an increased incidence among females with predominantly FVH. The current study provided much-needed information about the burden of Wilms' cancer in Yemen, to enable Yemen to better plan to address the burden. Further studies are necessary to determine the exact incidence and trend of Wilms' cancer and risk factors in Yemen.

Keywords: children's cancers, kidney cancers, Sana'a city, Wilms' tumor (WT), degree of anaplasia,

Introduction

Nephroblastoma, or Wilms' Tumor (WT), is an embryonic tumor of renal origin and is the most common genitourinary malignant tumor in children [1]. Overall, WT accounts for 7% of all childhood cancers and 90% of all pediatric tumors of the kidney [2]. WT is mostly unilateral however bilateral WT occurs in about 5% to 8% of patients [3]. In adults, WT accounts for less than 1% of all renal tumors [4]. Wilms' tumor affects 1 in 10,000 people worldwide before the age of 15 years [5]. People of African descent may have slightly higher rates of Wilms' tumor [5]. The maximum peak age of a Wilms tumor is 3 to 4 years and most cases occur before the age of 10 years. In Yemen, there are only some special epidemiological studies devoted to malignancies [6-13], although more research has been done on infectious and metabolic disorders in the past [14-22].

Wilms' tumor has many causes, which can generally be classified as syndromic and non-syndromic. The cause of Wilms tumor syndrome is caused by changes in genes such as the Wilms tumor 1 (WT1) genes or the Wilms tumor 2 (WT2) genes, and the tumor appears with a range of other signs and symptoms. Non-syndromic Wilms' tumor is not associated with additional symptoms or diseases. Many cases of Wilms' tumors develop from the anastomosis of the kidneys. Kidney pads are fragments of tissue in or around the kidney that arose before birth and turned into precancerous masses after birth. Cases of bilateral Wilms' tumor, in addition to cases of Wilms' tumor consequent from certain genetic syndromes for instance Denis-Drash syndrome, are generally closely associated with renal metastases. In cases of malignancy, it usually spreads to the lung. The rupture of a Wilms tumor puts the patient at risk of bleeding and the spread of peritoneal cancer cells. In such cases, surgical intervention by an experienced surgeon is necessary to remove such a fragile tumor [23,24].

The clinical presentation of WT usually includes an asymptomatic abdominal mass revealed incidentally by the parent, caregiver, or primary care physician. Other, non-specific clinical features include microscopic or gross hematuria, hypertension, abdominal pain, and fever [25]. Imaging tests for a WT scan entail an abdominal ultrasound, computed tomography (CT) scans and magnetic resonance imaging (MRI). However, CT scans should be carried out with concern in children due to the long-term negative effects of

radiation in children. Treatment for WT includes surgery and chemotherapy with or without radiation therapy. There are two treatment protocols for WT: the Children Oncology Group-National Wilms' Tumor Study Group (COG-NWTSG) protocol for primary surgery and the SIOP (International Society for Pediatric Oncology) protocol for advanced chemotherapy. Although there are many studies on WT conducted globally, there is a paucity of studies on WT in Sana'a, Yemen. Hence, we conducted this study aimed to describe the age, sex, and histology distribution of the Wilms tumor and its association with age groups, gender, and the kidney effected side; during the past eighteen years, based on data from two main pathology examination centers in Sana'a city, Yemen.

Subjects And Methods

A study designed: Retrospective descriptive study.

Study site: The unit of cancer in Al-Thorah University Hospital and the National Center for Public Health Laboratories (NCPHL) in the Departments of Pathology in Sana'a City which serve the major government hospitals and private hospitals in the city of Sana'a and act as reference laboratories for the entire country.

Study population: The study was conducted on renal lesion patients (patients are usually referred from hospitals for histological diagnosis) who were subsequently diagnosed selectively by histo-pathological study in the Department of Pathology at the National Center for Public Health Laboratories (NCPHL) and the unit of cancer in Al-Thorah University hospital Sana'a, Yemen, over a period of about 18 years from January 1, 2004, to December 31, 2021.

Operational variables: The cancer was classified according to the results of the tissue examination preserved in the paper records of each case before its entry into the SPSS program. The entry was reviewed by three different people to reduce the error during the entry of the collected data - and the sample size was determined by the number of patients diagnosed in the two selected units in the period between 2004 Until 2021, and the quality of the data was censured by excluding any record of patients who lacked any of the variables on which the research was based on.

Study variables and cancer classification: The variables of the study were the histological type of cancer, sex, grade, and age. Types, grades, and histological diagnoses were formed in line with the World Health Organization [26] and "Kidney Cancer, Version 2.2017,

NCCN Clinical Practice Guidelines in Oncology" [27].

Inclusion criteria: Inclusion criteria for patients included the following: complete renal histo-pathological findings, patients of any age and gender, availability of clinical data, and histological slides that confirm the diagnosis of kidney lesions and cancers.

Exclusion criteria: Patients with no histopathological slides and insufficient clinical data in the records were excluded.

Statistical analysis: Data were reported using suitable descriptive statistics (consisting of mean, frequency, standard deviation, OR, CI, X², and P-value). First data were entered using the SPSS software to minimize errors. All statistical analyzes of the data were performed using the Statistical Package for Social Sciences (SPSS) version 24 and Excel 2007.

Ethical approval: From the Faculty of Medicine and Health Sciences at Sana'a University, the Research and Ethics Committee with a reference number (811) dated 10-01-2022, the ethical approval was obtained. Also, all data, including patient identification, have been kept confidential.

Results

Malignant tumors counting 177/282 (62.8%) of the total kidney lesions, renal cell carcinoma (RCC) was the most predominant cancer counting 126/282 (44.7%), followed by Wilms tumors 47/282 (16.7%), while non-Hodgkin's lymphoma counting 3 cases (1.1%) and mucinous carcinoma one case (0.35%) (Table 1). Table 2 shows the sex and age distribution of 47 Wilms tumor patients. The female cases were 29/47 (61.7%) more than male cases 18/47 (38.3%). The mean age of the Wilms' patients was 5.3 years with SD equal to 3.6 years and ages ranged from 9 months to 15 years. Most of the Wilms' patients were in the age group 1-5 years 31/47(66%) followed by 6-10 years (25.5%), while in less than 1 year and >10 years groups there were only 2 cases (4.2%) in each group. Based on the degree of anaplasia in histology, Wilms tumor is divided into favorable histology and unfavorable histology, FVH, and UFVH, respectively. Table 3 shows the histology distribution of renal Wilms tumors among 47 children's patients; FVH Wilms tumors counted 42/47 (89.4%) while UFVH only counted 5/47 (10.6%). There was no significant association between Wilms' tumor and sex as there are approximately equal rates

in both sexes. Considering the age groups, there was a highly significant association of Wilms tumor with the 1–5-year group where the rate was 77.5% with OR = 48.6, CI = 19.8-119, $p < 0.001$.

Table 1: The distribution of different malignant tumors diagnosed between 2004-2022 in two centers in Sana'a, Yemen

Renal Lesions	Number	%
Malignant tumors	177	100
<i>Renal cell carcinoma</i>	126	71.2
<i>Wilms tumor</i>	47	26.6
<i>Non-Hodgkin's lymphoma</i>	3	1.7
<i>Mucinous carcinoma</i>	1	0.6

Table 2: Sex and age distribution of 47 Wilms tumor patients in Sana'a, Yemen

Characters	Number	%
Gender M:F ratio = 1.0: 1.6		
<i>Male</i>	18	38.3
<i>Female</i>	29	61.7
Age groups		
<i>Less than 1 year</i>	2	4.2
<i>1-5 years</i>	31	66
<i>6-10 years</i>	12	25.5
<i>>10 years</i>	2	4.2
Total	47	100
<i>Mean age</i>	5.3 years	
<i>SD</i>	3.6 years	
<i>Min</i>	9 months	
<i>Max</i>	15 years	
<i>Mode</i>	1 years	
<i>Median</i>	5 years	

Table 3: The histology distribution of renal Wilms tumor among 47 children's patients in Sana'a, Yemen.

Histology	Number	%
<i>FVH</i>	42	89.4
<i>UFVH</i>	5	10.6
Total	47	100

Table 4: The association between Wilms tumor (WT) with sex and ages among 282 renal lesions patients in Sana'a city, Yemen.

Characters		WT n=47 No (%)	OR	CI 95%	X ²	P
Gender						
Male n=124		18(14.5)	0.7	0.39-1.4	0.73	0.39
Female n=158		29 (18.4)	1.3	0.65-2.5	0.73	0.39
Age groups						
Less than 1 year	n=2	2 (100)	undefined	undefined	10.1	0.001
1-5 years n=40		31(77.5)	48.6	19.8-119	124	<0.001
6-10 years n=15		12 (80)	26.5	7.1-98.7	45.7	<0.001
>10 -15 years n=12		2(16.7)	1	0.2-4.7	0.0	1.0
Kidney side						
Right n=140		27 (19.2)	1.4	0.77-2.7	1.37	0.24
Left n=142		20(14.2)	0.7	0.37-1.3	1.2	0.26
Total n=282		47(16.7)				

OR = odd's ratio, CI 95% = confidence interval 95%, X² = Chi square, p= p value

Discussion

WT is the second most common intra-abdominal malignancy in children after neuroblastoma and WT arises from foci of persistent meta-nephric cells referred to as nephrogenic rests [25,28]. The formation of collaborative study groups and multimodal therapy has led to significant progress in the management of WT [29]. However, in developing countries, late presentation, malnutrition, poverty, and lack of multidisciplinary cooperation affect treatment outcomes for children with WT [30,31]. The two comprehensive collaborating groups that studied WT were the Pediatric Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP). In the current study, female cases were 29/47 (61.7%) more than male cases 18/47 (38.3%) (Table 2). The predominance of females recorded in this study is in agreement with the reports of Breslow *et al.* [32] and Kaste *et al.* [33] where female children were more prevalent in Wilm's tumors than male patients. However, Hadley *et al.* [31] and Davidson *et al.* [34] studies in Africa did not agree with current findings indicating a nearly identical incidence of Wilm's tumor in both sexes. Male/female predominance may depend on the geographical area of study. In the current study, the mean age of the Wilms patients was 5.3 ± 3.6 years and the patient's ages ranged from 9 months to 15 years; most of the Wilms patients were in the age group 1-5 years (66%) (Table

2). The present results differ from those reported by Breslow *et al.* [32] as there is no significant tendency for WT between the sexes; Its incidence and mean age at diagnosis are 1 in 10,000 and 3.5 years, respectively [32]. The mean age of 5.3 ± 3.6 years reported in the current study is also slightly older than the mean age of 4.5 years recently reported by Chukwubuike [23]. On the other hand, the current mean age of 5.3 ± 3.6 years is similar to that reported by Elayadi, *et al.* [35] in Egypt with an average age of 5.25 years. In the current study, two cases of WT were >10 years old (4.2%) (Table 2). This is again similar to Osuoji *et al.* [36] who reported a case of Wilms' tumor in a 12-year-old Nigerian female [36]. These differences can be explained by differences in race. It took an average of 6 months from the time the abdominal mass was noticed to the time the parents were presented to the hospital. This late presentation may explain why most of our patients (89.4%) have FVH Wilms tumors. Poverty and ignorance prevailing in developing countries can explain this late presentation [23]. The majority of our patients presented with FVH Wilms tumor with a better prognosis similar to other studies conducted in developing countries [37,38]. While UFVH Wilms tumor of poor prognosis was found in only 5 cases (10.6%). We found more right-sided WT than left-sided tumors (27 vs 20). This result differs from the report of Chukwubuike [23] and Ledlie *et al.* [39] where they found more left-sided WT than right-sided tumors. However, Wilde *et al.* [40] in

their series reported more right WT than left WT and this is similar to the results of our study. The reason for these differences is still unknown.

Limitations of the study

This study was limited by the small number of cases. A larger number of cases would have availed better analysis. This was a retrospective study. A perspective would have provided more information. Gene analyses of the patients were not done due to the non-availability of the necessary facilities.

Conclusion

WT is still associated with significant morbidity and mortality in resource-limited environments. Wilms tumors in Yemeni children appear at an early age and its peak in 1-5 years of life with an increased incidence among females with predominant FVH than UVFH. The current study provided much-needed information about the burden of Wilms cancer in Yemen, to enable Yemen to better plan to address the burden. Further studies are necessary to determine the exact incidence, trend of Wilms cancer, and risk factors in Yemen.

Author Contribution

This study was completed by Amin Abdulkarem Okbah, Professor of Histopathology at Sana'a University, and the National Center of Public Health Laboratories (NCPHL) Sana'a, Yemen; and Prof. Dr. Hassan Abdul-Wahab Al-Shamahy, Faculty of Medicine, Sana'a University. All authors analyzed the data, wrote the manuscript, and reviewed it.

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Conflict Of Interest

"No conflict of interest associated with this work".

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